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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,797	05/16/2001	James L. Hartley	0942.285000G	2106

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EXAMINER

SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/855,797

Applicant(s)
Hartley et al.

Examiner
William Sandals

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1636



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jan 16, 2003
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 52-68 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 52-68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on May 16, 2001 is/are a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4 6) ☐ Other:

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DETAILED ACTION

Status of the Claims

1. Claims 52-68 are pending. Claim 1 has been cancelled in Paper No. 7, filed January 16, 2003. Claims 1 and 52-68 were restricted in the office action mailed December 17, 2002 into Group I, claim 1, and Group II, claims 52-68. As a result of the cancellation of claim 1, the restriction is moot.
2. Claim 66 is objected to.
3. Claim 52 stands rejected under the judicially created doctrine of provisional obviousness double patenting over claim 56 of copending US Application 09/907,719.
4. Claims 57-59 and 60-63 stand rejected under 35 USC 112, second paragraph.
5. Claims 52-53 stand rejected under 35 USC 101, Lack of Utility.
6. Claims 52-55, 57 and 64-68 stand rejected as anticipated under 35 USC 102(b) over US 5,434,066 (Bebee et al.).
7. Claims 52-68 stand rejected as obvious under 35 USC 103(a) over US 5,434,066 (Bebee et al.) in view of US 5,929,307 (Hodges et al.) and further in view of Waterhouse et al.

Drawings

8. New formal drawings are required in this application because recent changes to the MPEP, section 608.02(c) no longer allow deferral of submission of drawings pursuant to

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notification. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the Patent and Trademark Office no longer prepares new drawings.

Claim Objections

9. Claim 66 is objected to because of the following informalities: Claim 66 recites "said at least of said one linear nucleic acid molecules" at line 2. The "of said" is an obvious typographical error, and should be deleted. Additionally, the recitation refers to the dependent claim 52 "at least one linear nucleic acid molecule", where "molecule" is singular. Pluralizing the word "molecule" to "molecules" in claim 66 is an obvious typographical error. Appropriate correction is required.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claim 52 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 56 of copending US Application No. 09/907,719. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claim 52 is drawn to a method for synthesizing one or more nucleic acid molecules comprising one or more recombination sites by adding adapters to one or both termini of a linear nucleic acid molecule, mixing the linear nucleic acid molecule which has adapters at the termini with a vector and a recombination protein, causing the recombination of the vector and linear molecule.

Claim 56 of US Application No. 09/907,719 is drawn to a method for synthesizing one or more nucleic acid molecules comprising one or more recombination sites by adding adapters to one or both termini of a linear nucleic acid molecule.

The method step of adding the adapters to the linear molecule is identical in both claims. It is not possible to practice the instant claimed invention of claim 52 without practicing the

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invention of US Application No. 09/907,719 claim 56, making the invention of US Application No. 09/907,719 claim 56 obvious over the instant invention of claim 52.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 101

12. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claims 52-53 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 53 is drawn to “genomic DNA”. A “genomic DNA” is a thing of nature, substantially unaltered, and is not a “manufacture”. Amending the claim to indicate the presence of the “hand of man” by adding words such as “isolated” or “purified” will cure this defect.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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15. Claims 52-55, 57 and 64-68 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,434,066 (Bebbee et al.).

Bebbee et al. teach a method for synthesizing one or more nucleic acid molecules comprising one or more recombination sites by adding adapters to one or both termini of a linear nucleic acid molecule, mixing the linear nucleic acid molecule which has adapters at the termini with a vector and a recombination protein, causing the recombination of the vector and linear molecule at column 4, lines 5-10 & 41-64 and columns 5 to column 7, line 10. The linear nucleic acid molecule is RNA, converted into cDNA or mechanically sheared genomic DNA as claimed in claim 55 (see column 4, lines 41-44 and example 4) to produce a library of nucleic acid molecules as recited in claims 67-68. The recombination protein was CRE or Int/Xis as claimed in claim 64 (see column 12, lines 48-63).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. Claims 52-57 and 64-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,434,066 (Bebbee et al.) in view of US 5,929,307 (Hodges et al.).

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The claims are drawn to a method for synthesizing one or more nucleic acid molecules comprising one or more recombination sites by adding adapters to one or both termini of a linear nucleic acid molecule, mixing the linear nucleic acid molecule which has adapters at the termini with a vector and a recombination protein, causing the recombination of the vector and linear molecule. Claims 53 and 54 recite that the linear nucleic acid is a genomic DNA molecule or a cDNA molecule. Claims 55 and 56 recite that the linear nucleic acid is produced by mechanical or enzymatic techniques. Claim 57 recites that adapters are added to both termini of the linear nucleic acid molecule. Claims 64 and 65 recite that the recombination protein is Cre, Int, IHF, Xis, or Fis. Claim 66 recites that the recombined vector comprises at least one linear nucleic acid. Claims 67-68 recite that the linear nucleic acid molecules are a population of molecules and a library of nucleic acid molecules.

Bebee et al. teach a method for synthesizing one or more nucleic acid molecules comprising one or more recombination sites by adding adapters to one or both termini of a linear nucleic acid molecule, mixing the linear nucleic acid molecule which has adapters at the termini with a vector and a recombination protein, causing the recombination of the vector and linear molecule at column 4, lines 5-10 & 41-64 and columns 5 to column 7, line 10. The linear nucleic acid molecule is RNA, converted into cDNA or mechanically sheared genomic DNA as claimed in claim 55 (see Bebee et al. at column 4, lines 41-44 and example 4) to produce a library of nucleic acid molecules as recited in claims 67-68. The recombination protein was CRE or Int/Xis as claimed in claim 64 (see Bebee et al. at column 12, lines 48-63).

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Hodges et al. teach a method for preparing a linear nucleic acid molecule for insertion into a vector by a recombination protein (see Hodges et al. at example 15). The linear nucleic acid molecule is a library of genomic DNA, which are enzymatically digested into linear DNA fragments (see Hodges et al. at column 15, bottom), and site-specific recombination sites are annealed, and enzymatically added to the termini.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the mechanically sheared genomic DNA of Bebee et al. with the enzymatically produced genomic DNA of Hodges et al. for the expected benefit of having single stranded termini which would anneal to adapters, thereby facilitating the ligation of the adapter to the linear molecule. Also, mechanically sheared DNA fragments and enzymatically produced DNA fragments are well known alternatives for production of genomic DNA fragments for insertion into a vector. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Bebee et al. and Hodges et al. in a method for synthesizing one or more nucleic acid molecules comprising one or more recombination sites by adding adapters to one or both termini of a linear nucleic acid molecule.

18. Claims 52-68 rejected under 35 U.S.C. 103(a) as being unpatentable over Bebee et al. and Hodges et al. as applied to claims 52-57 and 64-68 above, and further in view of Waterhouse et al.

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The claims are drawn to the invention described above, and also where the recombinase site-specific adapters ligated to the termini of the linear nucleic acid molecule are different at each termini as recited in claim 58. Claim 59 recites that the different site-specific adapters do not recombine with each other. Claim 60 recites that the vector comprises a second recombination site. Claim 61 recites that the different recombination sites are engineered recombination sites. Claims 62-63 recite that the different recombination sites are *att* or *lox* sites.

Bebee et al. and Hodges et al. teach the invention as described above.

Bebee et al. and Hodges et al. did not teach the recombinase site-specific adapters ligated to the termini of the linear nucleic acid molecule are different at each termini, nor that the different site-specific adapters do not recombine with each other, nor that the vector comprises a second recombination site, nor that the different recombination sites are engineered recombination sites.

Waterhouse et al. teach the creation (engineering) of different site-specific recombination sites at each end of a desired nucleic acid segment to insure the proper insertion of the desired segment in a target vector while avoiding deletion (see page 2265, col. 1, bottom, bridging to col. 2 top). The site-specific recombination sites at each end of the desired nucleic acid segment do not recombine. The vector comprises a second recombination site. (as recited in claims 58-61)

It would have been obvious to one ordinary skill in the art at the time of making the instant invention to substitute the site-specific recombination sites in the nucleic acid to be inserted into the vector of Bebee et al. with the non-recombining site specific recombination sites

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at each end of the nucleic acid to be inserted into the vector of Waterhouse et al. for the expected benefit of insuring proper insertion of the desired nucleic acid into the vector while avoiding deletion of the desired nucleic acid. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Bebee et al., Hodges et al. and Waterhouse et al. in a method for synthesizing one or more nucleic acid molecules comprising one or more recombination sites by adding adapters to one or both termini of a linear nucleic acid molecule where the site-specific termini are different and do not recombine.


Conclusion

19. Certain papers related to this application are *welcomed* to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Tech Center customer service center at telephone number (703) 308-0198.

William Sandals, Ph.D.


REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

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Examiner

March 30, 2003